European Patent Office

SUPPLEMENTARY PARTIAL EUROPEAN SEARCH REPORT

which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

Application Number EP 98 90 5708

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
X	SHARPE AH: "Analysis of lymphocyte costimulation in vivo using transgenic and 'knockout' mice" CURR OPIN IMMUNOL, vol. 7, no. 3, 1995, pages 389-395, XP001021014 * abstract * * page 391, left-hand column, paragraph 2 - page 393, left-hand column, paragraph 3 *	2-7,9, 10,12, 14-16, 19-21, 23,25-27	C07K14/705 C07K16/28 C07K9/00 C12N5/10 C12N15/12 C12P21/08 A01K67/027 A61K38/17 A61K39/395
Y		1-17, 19-27	

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TECHNICAL FIELDS SEARCHED (Int.Cl.6)

C07K

The supplementary search report has been based on the last set of claims valid and available at the start of the search.

INCOMPLETE SEARCH

The Search Division considers that the present application, or some or all of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for the following claims:

Claims searched completely :

Claims searched incompletely :

Claims not searched :

Reason for the limitation of the search:

see sheet C

Place of search	Date of completion of the search	Examiner
MUNICH	29 August 2001	Sommer, B

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C20)

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 98 90 5708

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	REDOGLIA V ET AL: "Characterization of H4: a mouse T lymphocyte activation molecule functionally associated with the CD3/Tcell receptor" EUR J IMMUNOL, vol. 26, 1996, pages 2781-2789, XP001013533 * abstract * * page 2783, right-hand column, paragraph 1 *	9,10,20, 21,23	
Y		1-17, 19-27	

X	NOJIMA Y ET AL: "The 4F9 Antigen is a member of the Tetra Spans Transmembrane protein family and functions as an accessory molecule in T cell activation and adhesion" CELLULAR IMMUNOL, vol. 152, 1993, page 249-260 XP001013534 * abstract *	2-4,6,7, 9,10,20, 21,23	TECHNICAL FIELDS SEARCHED (Int.Cl.6)

X	COCKS BG ET AL: "A novel receptor involved in T-cell activation" NATURE, vol. 276, 20 July 1995 (1995-07-20), pages 260-263, XP002923083 * abstract * * page 260, left-hand column, paragraph 2 - page 206, right-hand column, paragraph 2 * * page 263, left-hand column, paragraph 1 *	2-4,6,7, 9,10,20, 21,23	

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EPO FORM 1503 03.82 (P04C10)

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 98 90 5708

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
Y	KUCHROO V ET AL: "B7-1 and B7-2 costimulatory molecules activate differentially the Th1/Th2 developmental pathways: application to autoimmune disease therapy" CELL, vol. 80, 10 March 1995 (1995-03-10), pages 707-718, XP002166452 * abstract * * page 714, left-hand column, paragraph 2 - page 715, right-hand column, paragraph 1 *	20,21, 23-25	

X	TAI X ET AL.: "A role for CD9 molecules in T cell activation" J EXP MED, vol. 184, August 1996 (1996-08), pages 753-758, XP001013526 * abstract *	2,4-7,9, 10,20, 21,23	TECHNICAL FIELDS SEARCHED (Int.Cl.6)

T	TAMATANI T (REPRINT) ET AL: "AILIM/ICOS: a novel lymphocyte adhesion molecule" INTERNATIONAL IMMUNOLOGY, (JAN 2000) VOL. 12, NO. 1, PP. 51-55. PUBLISHER: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND ISSN: 0953-8178., XP001007236 JT INC, PHARMACEUT FRONTIER RES LABS, KANAZAWA KU, 1-13-2 FUKUURA, YOKOHAMA, KANAGAWA 236000, JAPAN (Reprint) * the whole document *	1-17, 19-27	

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European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 98 90 5708

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
T	TEZUKA K (REPRINT) ET AL: "Identification and characterization of rat AILIM/ICOS, a novel T-cell costimulatory molecule, related to the CD28/CTLA4 family" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (16 SEP 2000) VOL. 276, NO. 1, PP. 335-345. PUBLISHER: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495. ISSN: 0006-291X., XP000999375 JT INC, PHARMACEUT FRONTIER RES LABS, KANAZAWA KU, FUKUURA 1-13-2, KANAGAWA 2360004, JAPAN (Reprint) * the whole document * -----	1-17, 19-27	TECHNICAL FIELDS SEARCHED (Int.Cl.6)

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INCOMPLETE SEARCH
SHEET C

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Claim(s) searched incompletely:
1-17, 19-27

Reason for the limitation of the search:

Claims 1, 2, 10-12, 14, 16, 20-22 and 23 are unclear due to the vague and indefinite terms "fragment", "epitope-bearing portion", "extracellular region" or "portion thereof". The same applies to claims 3-9, 11, 13, 15-17, 19-21 and 23-27, as far as they refer to the aforementioned claims. It is not unambiguosly derivable from the description and in particular the claims, which polypeptides or nucleic acids, respectively, fall within the scope of said claims, as such compounds can only be defined by technical features, i.e. their exact sequence. Therefore, only an incomplete search has been performed for claims 1-17 and 19-21 based on either the full-length SEQ ID Nos. 1-6, or those fragments of SEQ ID No. 3-6 which are indicated in claim 2(d). With respect to fragments etc. in general, the scope of the claims is completely unclear and cannot be searched.
Moreover, the effect of an antibody produced by a deposited hybridoma in claim 22 is not defined by technical features. It is therefore unclear, what is meant by "substantially the same effect". For the purpose of an incomplete search, this feature was interpreted as in claim 1b) and c).

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CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☒ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☐ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

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LACK OF UNITY OF INVENTION
SHEET B

Application Number
EP 98 90 5708

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 1, 2, 4-7 , 9-16 , 20-26 (all partially); 3, 8, 17 and 19 (completely)

A nucleic acid encoding a human T-cell surface molecule and having either the coding sequence shown in SEQ ID No. 1 or 3 (residues 26-625), respectively, or encoding a polypeptide having the amino acid sequence SEQ ID No. 2 as well as subject-matter related thereto.

2. Claims: 1, 2, 4-7, 9-16, 20-26 (all partially)

A nucleic acid encoding either a rat T-cell surface molecule or a splicing variant thereof and having the coding sequence shown in SEQ ID No. 4 (residues 35-637) or SEQ ID No. 6 (residues 35-685), respectively, as well as subject-matter related thereto.

3. Claims: 1, 2, 4-7, 9-16, 20-25 (all partially); 27 (completely)

A nucleic acid encoding a murine T-cell surface molecule and having the coding sequence shown in SEQ ID No. 5 as well as subject-matter related thereto.

The only common concept linking the three groups of inventions is that of providing costimulatory cell surface molecules having the features as disclosed in claim 1a)- c). However, said concept is not novel, as molecules like CD28 or CTLA-4 are covered by that concept. Due to the fact, that claim 2 is much broader than claim 1 and covers peptides with completely unrelated primary structures, the two sequence motifs mentioned in claim 1d)-e) cannot constitute an unifying feature, as the claimed molecules do no necessarily comprise those specific motifs. Consequently, there is a lack of unity and each of the groups of claims defined above constitutes a separate invention.

CLAIMS

1. A polypeptide constituting a cell surface molecule having characteristics below:

(a) said cell surface molecule is expressed in at least thymocytes and mitogen-stimulated lymphoblast cells;

(b) an antibody reactive to said cell surface molecule induces adhesion between mitogen-stimulated lymphoblast cells;

(c) an antibody reactive to said cell surface molecule induces proliferation of peripheral blood lymphocytes in the presence of an antibody against CD3;

(d) said cell surface molecule has a partial amino acid sequence represented by Phe-Asp-Pro-Pro-Pro-Phe in its extracellular region; and

(e) said cell surface molecule has a partial amino acid sequence represented by Tyr-Met-Phe-Met in its cytoplasmic region.

2. The polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO: 2 or the amino acid sequence of SEQ ID NO: 2 in which one or more amino acids are substituted, deleted, or added.

3. The polypeptide of claim 1, which is encoded by a DNA hybridizing with a DNA having the nucleotide sequence of SEQ ID NO: 1 under stringent conditions.

4. The polypeptide of claim 1, comprising an amino acid sequence having 60% or more homology with an amino acid sequence of SEQ ID NO: 2.

5. The polypeptide of any one of claims 1 to 4, wherein said cell surface molecule is derived from human.

6. A gene encoding the polypeptide of any one of claims 1 to 5.

7. The gene of claim 6, wherein said gene is a cDNA.

8. The gene of claim 7, wherein said cDNA has a nucleotide sequence of SEQ ID NO: 1.

9. The gene of claim 7, wherein said cDNA comprises a nucleotide sequence corresponding to nucleotide residues 26 to 625 of SEQ ID NO: 3, nucleotide residues 35 to 637 of SEQ ID NO: 4, nucleotide residues 1 to 603 of SEQ ID NO: 5, or nucleotide residues 35 to

685 of SEQ ID NO: 6.

10. A vector comprising the gene of any one of claims 6 to 9.

11. A transformant into which the vector of claim 10 has been introduced.

12. A transformant identified by an international deposit accession No. FERM BP-5725.

13. A polypeptide fragment comprising an extracellular region of the polypeptide of any one of claims 1 to 5.

14. The polypeptide fragment of claim 13, wherein said polypeptide is a human-derived polypeptide having an amino acid sequence of SEQ ID NO: 2.

15. A gene encoding the polypeptide fragment of claim 13 or 14.

16. A homodimer molecule comprising two polypeptide fragments, wherein each of the fragments comprises an extracellular region of the polypeptide of any one of claims 1 to 5 and said two polypeptide fragments bridged through disulfide bonds to each other.

17. The homodimer molecule of claim 16, wherein said polypeptide is a human-derived polypeptide having an amino acid sequence of SEQ ID NO: 2.

18. A pharmaceutical composition comprising either of the polypeptide fragment of claim 14 or the homodimer molecule of claim 17, or both of them, and a pharmaceutically acceptable carrier.

19. A fusion polypeptide comprising an extracellular region of the polypeptide of any one of claims 1 to 5 and a constant region of a human immunoglobulin (Ig) heavy chain or a portion of the constant region.

20. The fusion polypeptide of claim 19, wherein the immunoglobulin is IgG.

21. The fusion polypeptide of claim 19, wherein the portion of the constant region comprises a hinge region, C2 domain, and C3 domain of IgG.

22. The fusion polypeptide of any one of claims 19 to 21, wherein said polypeptide is a human-derived polypeptide having an amino acid sequence of SEQ ID NO: 2.

23. A homodimer molecule comprising two fusion polypeptides of

any one of claims 19 to 22 wherein the two polypeptides bridged through disulfide bonds to each other.

24. A homodimer molecule comprising two fusion polypeptides of claim 22 wherein the two polypeptides bridged through disulfide bonds to each other.

25. A pharmaceutical composition comprising either of the fusion polypeptide of claim 22 or the homodimer molecule of claim 24, or both of them, and a pharmaceutically acceptable carrier.

26. The pharmaceutical composition of claim 25, wherein said pharmaceutical composition is utilized for treating autoimmune diseases or allergic diseases, or for preventing said disease symptom.

27. An antibody or a portion thereof reactive to the polypeptide of any one of claims 1 to 5, the polypeptide fragment of claim 13 or 14, or the cell surface molecule comprising said polypeptide.

28. The antibody of claim 27 or a portion thereof, wherein said antibody is a monoclonal antibody.

29. A monoclonal antibody or a portion thereof reactive to the polypeptide having an amino acid sequence of SEQ ID NO: 2, the polypeptide fragment of claim 14, or the human-derived cell surface molecule comprising said polypeptide.

30. A monoclonal antibody or a portion thereof rective to the polypeptide of any one of claims 1 to 5 or the cell surface molecule comprising said polypeptide, wherein the effect of said monoclonal antibody on mitogen-stimulated lymphoblast cells is substantially the same as the effect of a monoclonal antibody produced by a hybridoma identified by an international deposit accession No. FERM BP-5707 on mitogen-stimulated rat lymphoblast cells.

31. A monoclonal antibody or a portion thereof rective to the polypeptide of any one of claims 1 to 5 or the cell surface molecule comprising said polypeptide, wherein the effect of said monoclonal antibody on mitogen-stimulated lymphoblast cells is substantially the same as the effect of a monoclonal antibody produced by a hybridoma identified by an international deposit accession No. FERM BP-5708 on mitogen-stimulated rat lymphoblast cells.

32. A pharmaceutical composition comprising the monoclonal

antibody of claim 29 or a portion thereof and a pharmaceutically acceptable carrier.

33. The pharmaceutical composition of claim 32, wherein said pharmaceutical composition is utilized for treating autoimmune diseases or allergic diseases, or for preventing said disease symptom.

34. A hybridoma producing the monoclonal antibody of any one of claims 28 to 31.

35. A transgenic mouse in which a gene encoding the polypeptide of claim 1 is integrated into its endogenous gene, wherein said gene is a human-derived gene comprising a nucleotide sequence of SEQ ID NO: 1 or a rat-derived gene comprising a nucleotide sequence corresponding to nucleotide residues 35 to 637 of SEQ ID NO: 4.

36. A knockout mouse in which its endogenous gene encoding the mouse polypeptide of claim 1 comprising the amino acid sequence encoded by the gene of SEQ ID NO: 5 is inactivated so that said mouse polypeptide is not produced.